

Pear Therapeutics: Redefining Medicine

Prescription Digital Therapeutics for the
Treatment of Serious Disease

reSET® and reSET-O®

Substance Use Recovery Task Force
November 10, 2020 Frankfort, KY

Yuri Maricich, MD, MBA Chief Medical Officer

Alex Waldron, Chief Strategy Officer



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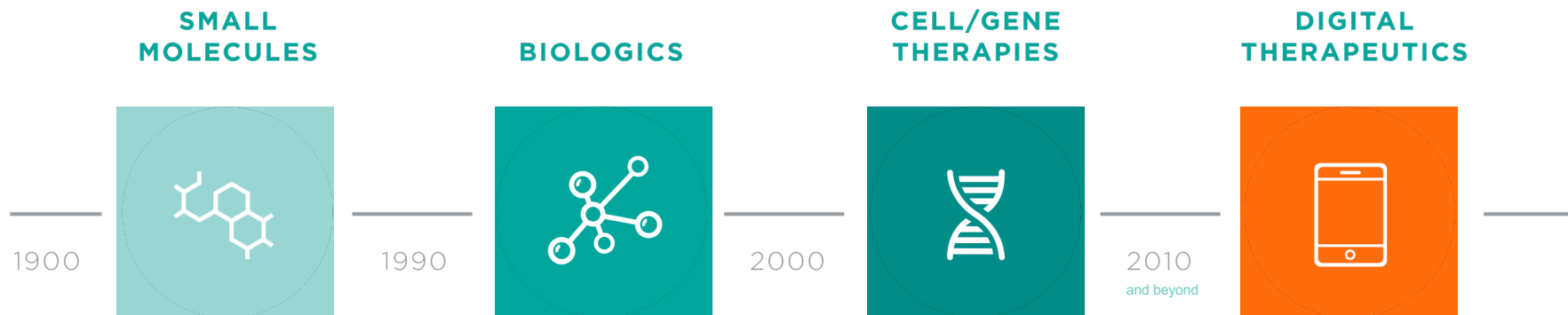
Agenda

Prescription Digital Therapeutics

- Pear Therapeutics
- SUD / OUD
- reSET and reSET-O



Prescription Digital Therapeutics (PDTs): a new therapeutic class that is being integrated into standard of care



“Software as therapeutics” that treat serious diseases with high unmet medical need

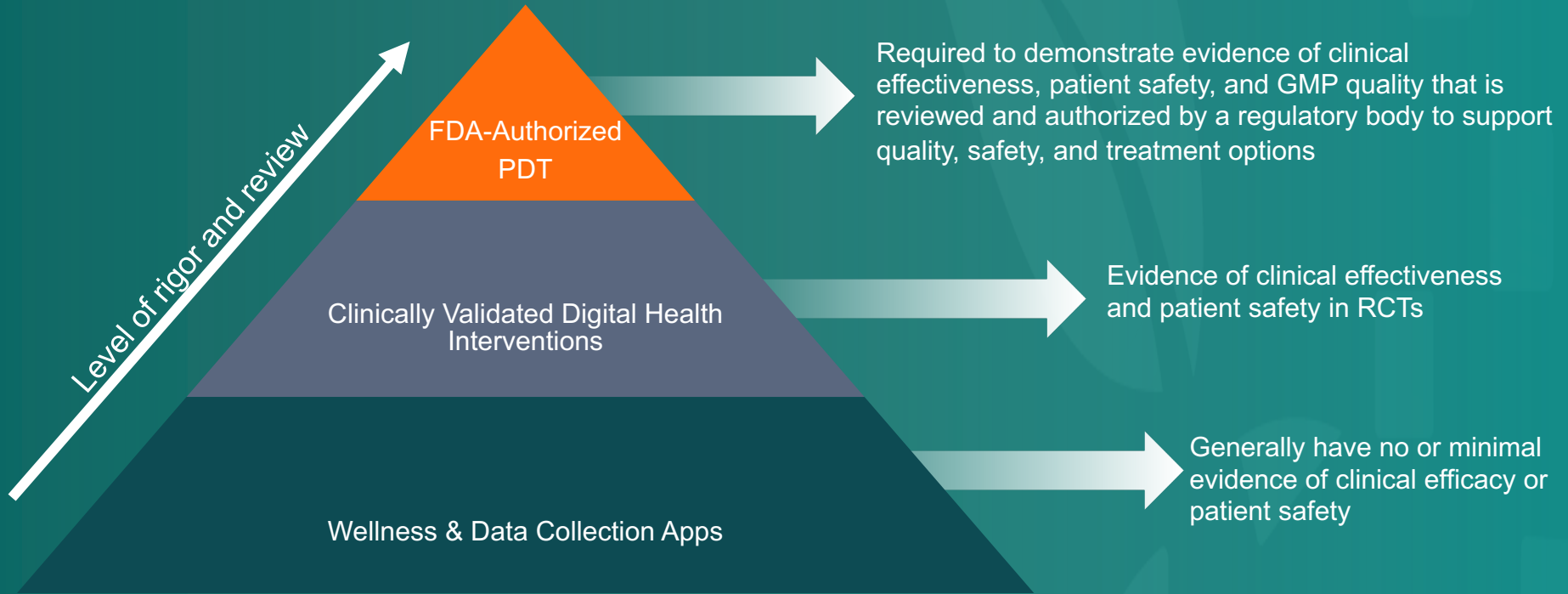
PDTs meet stringent regulatory requirements related to:

- Safety and effectiveness of clinical data ^{1,2}
- Regulatory labeling³
- Payers to evaluate coverage based on traditional therapeutic coverage mechanisms

1. Campbell ANC, Nunes EV, Matthews AG, et al. Internet-delivered treatment for substance abuse: a multisite randomized controlled trial. *Am J Psychiatry*. 2014;171(6):683-690.
2. Christensen DR, Landes RD, Jackson L, et al. Adding an internet-delivered treatment to an efficacious treatment package for opioid dependence. *J Consult Clin Psychol*. 2014;82(6):964-972.
3. Federal Drug Administration permits marketing of mobile medical application for substance use disorder [press release]. FDA News Release; Site <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm576087.htm> Published September 14, 2017. Accessed July 2019



What is a Prescription Digital Therapeutic (PDT)?

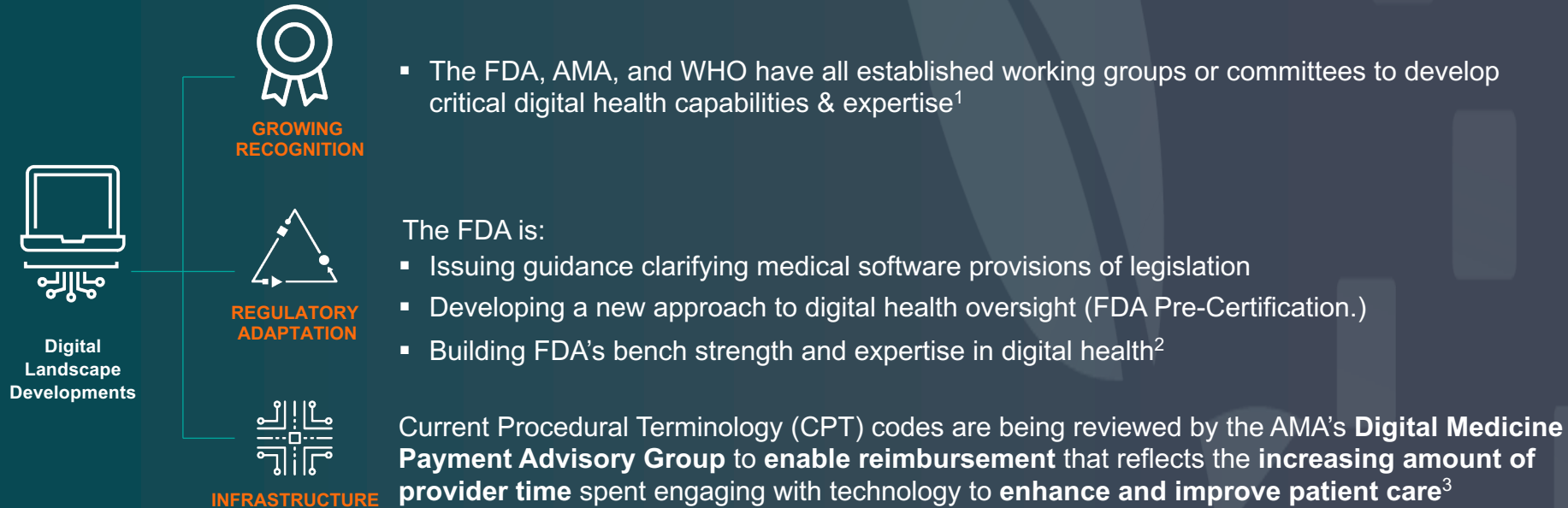


PDTs have efficacy and safety data in FDA authorized label

	Prescription Digital Therapeutics (PDTs)	Traditional Wellness Apps
Deliver disease-specific, evidence-based treatment via mobile devices	✓	✗
FDA-regulated software as a medical device (SaMD)	✓	✗
Evaluated and clinically-validated for safety and efficacy	✓	✗
Receive FDA-marketing authorization	✓	✗
Intended to be used as adjunct to standard outpatient treatment	✓	✗
Label describes indications and intended use, supporting appropriate clinical use	✓	✗



PDT Landscape Gaining Momentum



1. World Health Organization News Release. WHO is establishing technical advisory group and roster of experts on digital health. Published 2019. Website: <https://www.who.int/news-room/detail/10-05-2019-who-is-establishing-technical-advisory-group-and-roster-of-experts-on-digital-health>. Accessed July 2019

2. AMA News Release. Henrey, Tanya Albert. 2019 CPT codes offer new paths to payment for digital medicine. Published October 17, 2018. Website: <https://www.ama-assn.org/practice-management/cpt/2019-cpt-codes-offer-new-paths-payment-digital-medicine>. Accessed 2019

3. Federal Drug Administration. Precertification (Pre-Cert) Pilot Program: Frequently Asked Questions. Updated July 2019. Website <https://www.fda.gov/medical-devices/digital-health-software-precertification-pre-cert-program/precertification-pre-cert-pilot-program-frequently-asked-questions>. Accessed July 2019



Agenda

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Pear Therapeutics

- SUD / OUD
- reSET and reSET-O



Pear is partnering for healthcare transformation



Partnering for Innovation

PROVIDER LEADERSHIP

Novel approach to patient care

CONNECTIVITY TO PATIENTS

Track patient engagement to treatment and highlight areas of need through Clinician Dashboard

PATIENT ACCESS & ENGAGEMENT

Support patients through novel treatment option with 24/7 access



Clinically Meaningful Outcomes

PATIENT OUTCOMES

Deliver reliable and clinically-validated therapeutics

EFFICACY & SAFETY

Focused on developing PDTs with proven efficacy and safety through RCTs.

DATA DRIVING CLINICAL INSIGHT

Track patient cravings, triggers, severity and drug use in real-time through the Clinician Dashboard



Attaining Value-Based Care

COST SAVINGS

May decrease healthcare cost savings, for example, ED visit frequency and excess non-OD treatment costs for patients with OUD

PATIENT ENGAGEMENT

May decrease patient no-shows and multiple bookings, while increasing patient adherence and compliance



Pear PDTs Follow the Traditional Therapeutics Model

Product



Therapeutic with effectiveness claims to treat disease



Software with effectiveness claims to treat disease

Prescription



Patient diagnosed by physician and product is prescribed

Payment



Reimbursed via pharmacy or medical benefit

Fulfillment



Dispensed via a specialty pharmacy/Patient Service Center

Use



Patient uses product according to indications for use

Follow-up



Patient follows up with physician



Agenda

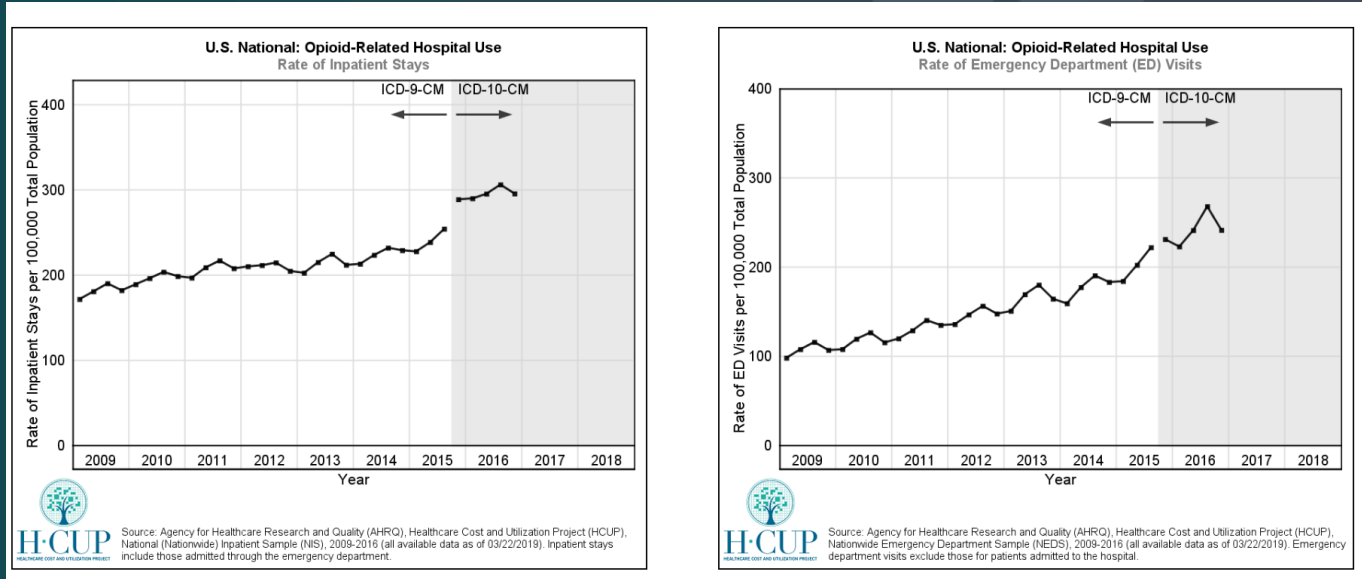
- Prescription Digital Therapeutics
- Pear Therapeutics

SUD / OUD

- reSET and reSET-O



Opioid use drives high cost inpatient hospital stays & ED visits



Source: Healthcare Cost and Utilization Project
<https://www.hcup-us.ahrq.gov/faststats/OpioidUseServlet?radio-3=on&location1=US&characteristic1=01&setting1=IP&location2=US&characteristic2=01&setting2=ED&expansionInfoState=hide&dataTableState=hide&definitionsState=hide&exportState=hide>



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- Prescription Digital Therapeutics
- Pear Therapeutics
- SUD / OUD

reSET and reSET-O



reSET[®] and reSET-O[®] were developed to address challenges with SUD / OUD treatment

reSET[®] is derived from the content of the Therapeutic Education System (TES), developed by Lisa Marsch, PhD, at Dartmouth's Geisel School of Medicine

- TES was developed in response to NIH solicitation for projects to digitize evidence-based behavioral therapies
- TES is an interactive, web-based program rooted in the evidence-based Community Reinforcement Approach to behavior therapy¹
- reSET delivers TES content via a mobile app, rather than a desktop computer

reSET's digital delivery method is designed to:



Increase Engagement And Retention



Improve Patient Access To Treatment

1. Bickel et al. Exp Clin Psychopharmacol. 2008;16(2):132-143.



Engage patients and clinicians to treat Substance Use Disorder

reSET®

INTERVENTION

Cognitive Behavioral
Therapy (CBT)
Modules

Fluency Training

Contingency
Management

Craving &
Trigger Assessment



reSET®

INSIGHT

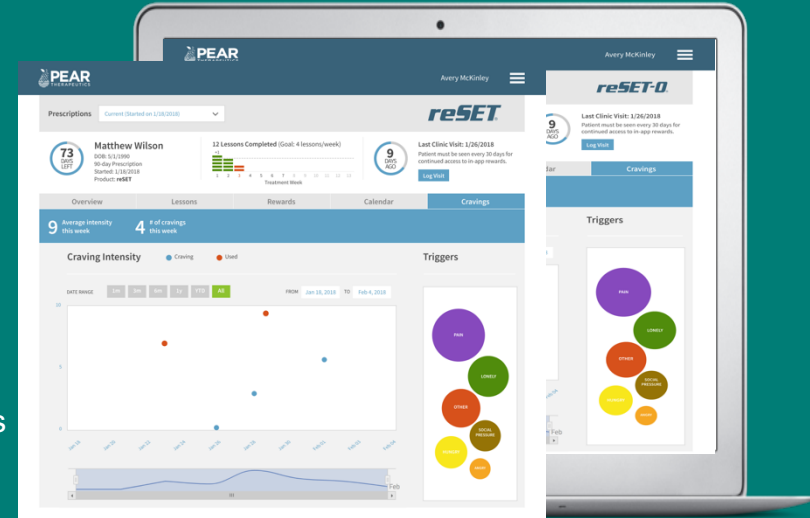
Abstinence and
Appointments

CBT Module Use

Fluency Training

Contingency
Management

Cravings and Triggers



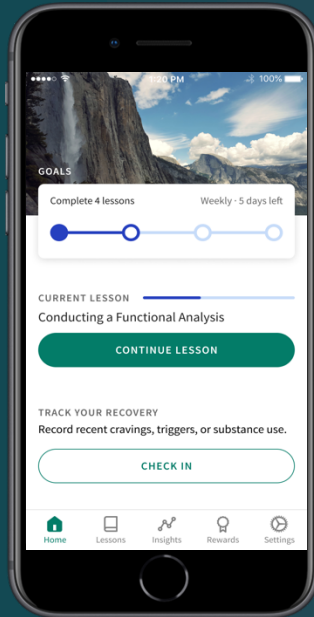
PATIENT

CLINICIAN

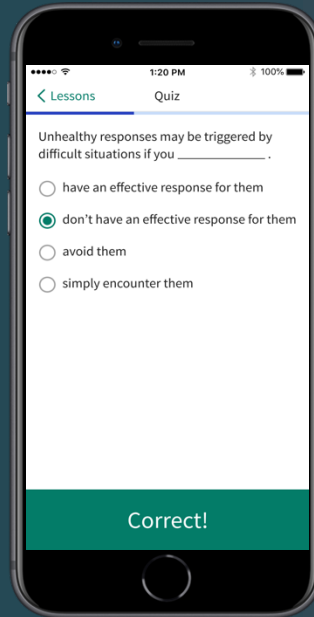


Implementing therapeutic techniques designed to maximize clinical effectiveness

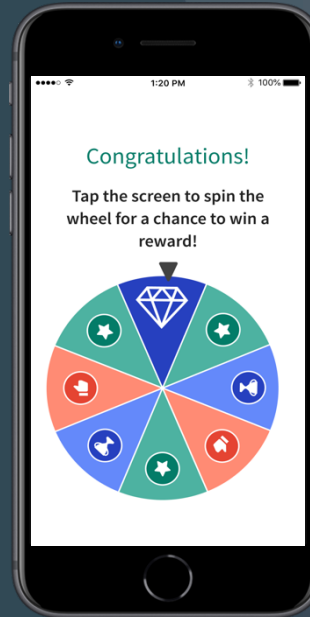
Cognitive Behavioral Therapy (CBT) Lessons



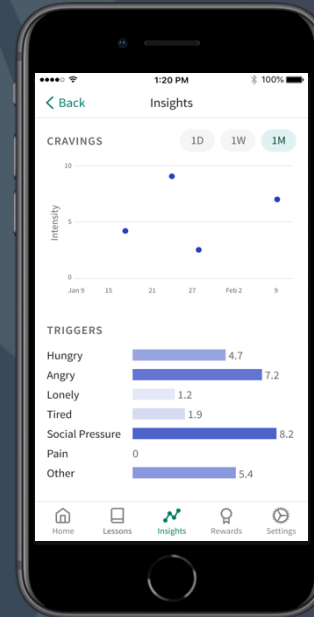
Fluency Training



Contingency Management



Craving & Trigger Assessment



reSET®: Revolutionary paradigm to treat Substance Use Disorder

INDICATION(S)

- reSET® is intended to provide cognitive behavioral therapy, as an adjunct to a contingency management system, for patients 18 years of age and older, enrolled in outpatient treatment under the supervision of a clinician
- 12-week prescription duration
- Patient population: Patients with SUD, under treatment for the following:
 - Stimulants, Alcohol + another substance, Marijuana, Cocaine, Opioids (when not primary substance of abuse)
- Not indicated for patients who are on opioid replacement therapy, or abusing alcohol solely, or abusing opioids as their primary substance

MECHANISM OF ACTION

Delivers therapy based on the community reinforcement approach (CRA), an intensive form of validated neurobehavioral therapy for SUD, along with contingency management and fluency training to enhance learning.

PRODUCT DESCRIPTION

- Based on the Therapeutic Education System (TES)
- Comprised of 62 interactive modules: 32 core modules and 30 supplemental modules
- Core modules focus on key CRA concepts, building skills to support behavior change and prevent relapse
- Supplemental modules provide more in-depth information on specific topics such as relationship skills or living with Hepatitis C
- Each module can be completed in approximately 10-20 minutes

1. American Journal of Psychiatry. 2014. 171(6):683-690.
2. Pear Internal data and Pear regulatory submission. DEN160018

3. Campbell et al., American Journal of Psychiatry. 2014. 171(6):683-690.
4. Chaple et al. 2016. The Prison Journal. 96(3):485-508.
5. DEN 160018 FDA Decision Summary.



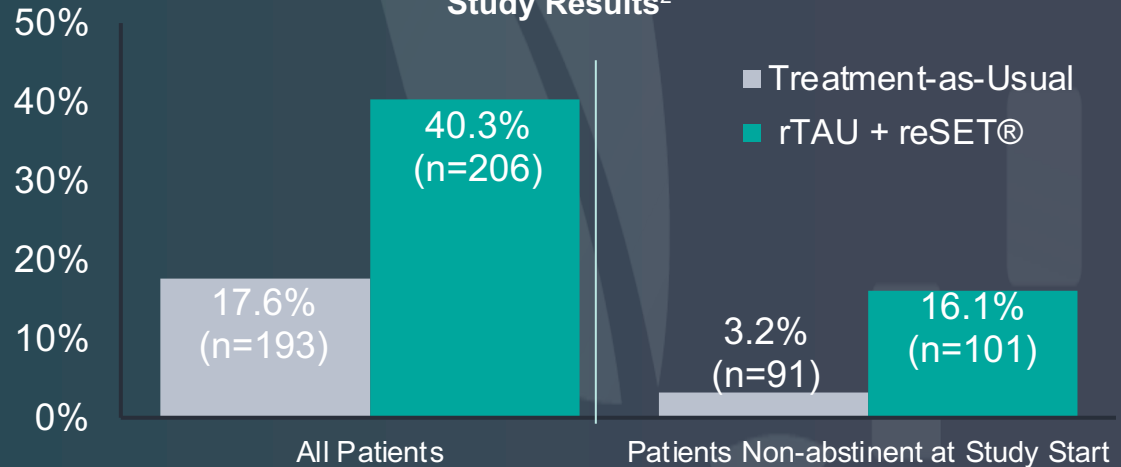
reSET Clinical Data | Pivotal Trial Summary

PIVOTAL TRIAL OVERVIEW

- 399 patients with SUD (alcohol, cannabis, cocaine, stimulants) received either:
 - Treatment-as-Usual (TAU), consisting of intensive face-to-face therapy
 - Reduced TAU and reSET (rTAU+reSET®) for 12 weeks¹
- Patients provided urine samples twice per week to objectively monitor abstinence
- Co-primary study endpoints
 - Abstinence in weeks 9-12
 - Retention in treatment

1. American Journal of Psychiatry. 2014; 171(6):683-690.
2. Pear Internal data and Pear regulatory submission. DEN160018

Study Results²



Outcomes	rTAU+reSET®	TAU	P-value
Abstinence: all patients	40.3%	17.6%	0.0004
Abstinence: non-abstinent at study start	16.1%	3.2%	0.0013
Retention in treatment: all patients	76.2%	63.2%	0.0042



reSET | Additional Clinical Data Highlights

HIGHLIGHTS

CLINICAL OUTCOMES SUMMARY

Abstinence

- Among patients whose primary addiction was not opioids, adding reSET® to outpatient therapy more than doubled abstinence rates (40% vs. 18%)

Retention

- Among all patients, adding reSET® to outpatient therapy improved rates of retention (76% vs. 63%)
- Patients who adhered to reSET® module completion in the first six weeks of the trial were 7x more likely to complete treatment than those who did not

Treatment Attendance

- Clinical trial data revealed a positive correlation between module completion and appointment attendance¹

Safety

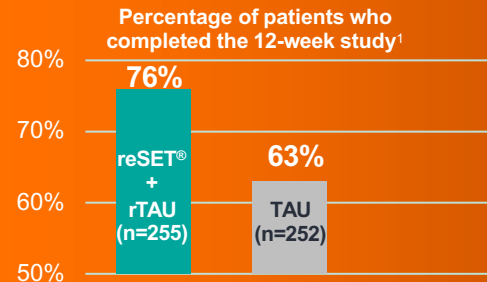
- reSET® did not demonstrate a significant difference in unanticipated adverse events¹

Module Completion

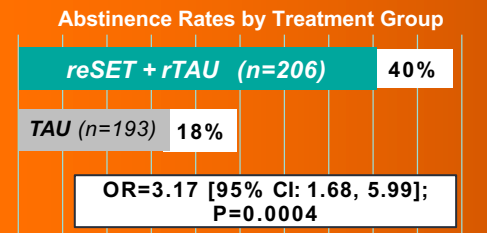
- Average Core Modules Completed: 38² (of 48)
- Number of reSET® modules completed correlated with abstinence ($R^2=0.21$, $p<.001$ with $n=206$)²

1. Pear Internal data and Pear regulatory submission, DEN160018
 2. Luderer HF, Campbell ANC, Nunes EV, Marichich YA. A Digital Therapeutic for SUD, reSET®, Demonstrates a Correlation Between Dose and Treatment Outcomes. Poster presented at: 29th Annual Meeting of the American Academy of Addiction Psychiatry; December 6-9, 2018; San Diego, CA.

Retention



Abstinence



[†]Among patients whose primary addiction was not opioids



reSET-O®: Revolutionary paradigm to treat Opioid Use Disorder



INDICATION(S)

- reSET-O® is intended to increase retention of patients with opioid use disorder (OUD) in outpatient treatment by providing cognitive behavioral therapy, as an adjunct to outpatient treatment that includes transmucosal buprenorphine and contingency management, for patients 18 years or older who are currently under the supervision of a clinician.
- 12-week prescription duration
- Indicated as a prescription-only digital therapeutic

MECHANISM OF ACTION

- Delivers addiction-specific form of CBT, fluency training, and contingency management for opioid use disorder (OUD)

PRODUCT DESCRIPTION

- Based on the Therapeutic Education System (TES)
- Comprised of 67 interactive modules: 31 core modules and 36 supplemental modules
- Core modules focus on key CRA concepts, building skills to support behavior change and prevent relapse
- Supplemental modules provide more in-depth information on specific topics such as relationship skills or living with hepatitis
- Each module is approx. 10-20 minutes
- Voluntary buprenorphine check-in feature to support buprenorphine use

1. American Journal of Psychiatry. 2014. 171(6):683-690.
2. Pear Internal data and Pear regulatory submission. DEN160018

3. Campbell et al., American Journal of Psychiatry. 2014. 171(6):683-690.
4. Chaple et al. 2016. The Prison Journal. 96(3):485-508.
5. DEN 160018 FDA Decision Summary.



reSET-O Clinical Data | Pivotal Trial Summary

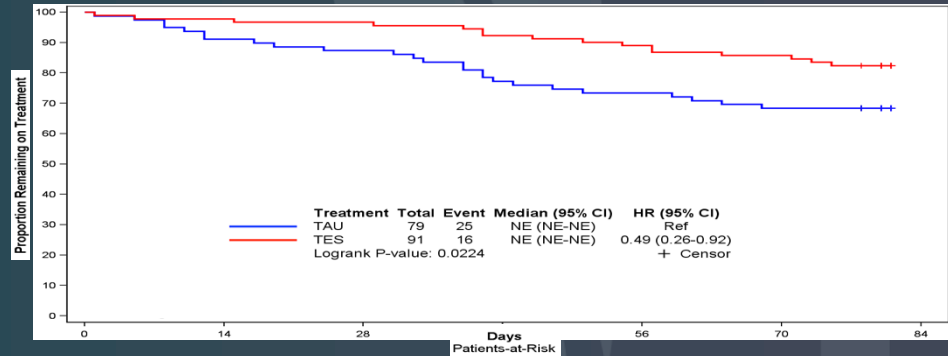
PIVOTAL TRIAL OVERVIEW

- 170 patients were randomized to receive either:
 - Treatment-as-Usual (TAU), consisting of Contingency Management + buprenorphine¹ or
 - TAU + reSET-O[®] (academic name Therapeutic Education System, or TES) + Contingency Management + buprenorphine
- All patients received 30 mins. of face-to-face counseling every other week.
- Patients provided urine samples 3x per week to objectively monitor abstinence.
- Co-primary endpoint analysis²
 - Negative urine drug screens in weeks 9-12
 - Retention in treatment

1. Christensen DR, Landes RD, Jackson L, et al. Adding an internet-delivered treatment to an efficacious treatment package for opioid dependence. J Consult Clin Psychol. 2014;82(6):964-972. doi:10.1037/a0037496., and Pear regulatory submission. DEN160018hcf, and reSET-O Clinician Directions for Use. Boston, MA: Pear Therapeutics, Inc; 2019.

2. Pear regulatory submission. DEN160018hcf

STUDY RESULTS¹



	TAU + reSET-O [®]	TAU	P-value
Retention (All)	82.4%	68.4%	0.0067



reSET-O | Additional Clinical Data Highlights¹

HIGHLIGHTS	CLINICAL OUTCOMES SUMMARY
Retention	<ul style="list-style-type: none">Adding reSET-O[®] to outpatient treatment using buprenorphine increased retention of patients with OUD almost 15%
Safety	<ul style="list-style-type: none">The observed adverse events (AE) were of type and frequency as anticipated in a large population of patients with OUD, or associated with buprenorphine pharmacotherapy, particularly during the induction phase.The AEs observed were not adjudicated to be device related.reSET-O[®] vs TAU did not demonstrate any significant safety differences between the cohorts

1. Christensen DR, Landes RD, Jackson L, et al. Adding an internet-delivered treatment to an efficacious treatment package for opioid dependence. J Consult Clin Psychol. 2014;82(6):964-972. doi:10.1037/a0037496., and Pear regulatory submission. DEN160018hcf, and reSET-O Clinician Directions for Use. Boston, MA: Pear Therapeutics, Inc; 2019.



Indications for Use

reSET is intended to provide cognitive behavioral therapy, as an adjunct to a contingency management system, for patients 18 years of age and older who are currently enrolled in outpatient treatment under the supervision of a clinician. reSET is indicated as a 12-week (90 days) prescription-only treatment for patients with substance use disorder (SUD), who are not currently on opioid replacement therapy, who do not abuse alcohol solely, or who do not abuse opioids as their primary substance of abuse.

It is intended to:

- Increase abstinence from a patient's substances of abuse during treatment, and
- Increase retention in the outpatient treatment program.

Important Safety Information

Warnings: reSET is intended for patients whose primary language is English and who have access to an Android/iOS tablet or smartphone. reSET is intended only for patients who own a smartphone and are familiar with use of smartphone apps (applications).

Clinicians should not use reSET to communicate with their patients about emergency medical issues. Patients should be clearly instructed not to use reSET to communicate to their clinician any urgent or emergent information. reSET is not to be used for emergencies. In case of an emergency, patients should dial 911 or go to the nearest emergency room.

reSET is not intended to be used as a stand-alone therapy for substance use disorder (SUD) and does not replace care by a licensed medical practitioner. reSET does not represent a substitution for a patient's medication. Patients should continue to take their medications as directed by their physician or medical provider.

The long-term benefit of treatment with reSET on abstinence has not been evaluated in studies lasting beyond 12 weeks in the Substance Use Disorder (SUD) population. The ability of reSET to prevent potential relapse after treatment discontinuation has not been studied.

This presentation does not include all the information needed to use reSET safely and effectively. Please see full Directions for Use for complete Important Safety Information.



reSET-O[®]

Indications for Use:

reSET-O is intended to increase retention of patients with opioid use disorder (OUD) in outpatient treatment by providing cognitive behavioral therapy, as an adjunct to outpatient treatment that includes transmucosal buprenorphine and contingency management, for patients 18 years or older who are currently under the supervision of a clinician. reSET-O is indicated as a prescription-only digital therapeutic.

Important Safety Information

Warnings: reSET-O is intended for patients whose primary language is English and who have access to an Android/iOS tablet or smartphone. reSET-O is intended only for patients who own a smartphone and are familiar with use of smartphone apps (applications).

Clinicians should not use reSET-O to communicate with their patients about emergency medical issues. Patients should be clearly instructed not to use reSET-O to communicate to their clinician any urgent or emergent information. In case of an emergency, patients should dial 911 or go to the nearest emergency room.

reSET-O is not intended to be used as a stand-alone therapy for Opioid Use Disorder (OUD). reSET-O does not replace care by a licensed medical practitioner. reSET-O does not represent a substitution for a patient's medication. Patients should continue to take their medications as directed by their healthcare provider. The ability of reSET-O to prevent potential relapse after therapy discontinuation has not been studied.

This presentation does not include all the information needed to use reSET-O safely and effectively. Please see full Directions for Use for complete Important Safety Information.



References

1. reSET® Clinician Directions for Use. Boston, MA and San Francisco, CA. Pear Therapeutics; 2019.
2. reSET-O® Clinician Directions for Use. Boston, MA and San Francisco, CA. Pear Therapeutics; 2019.

